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Anesthetic Considerations in McCune-Albright Syndrome: Case Report with Literature Review

Robert A. Langer, MD, Inkyoon Yook, MD, and Levon M. Capan, MD

Department of Anesthesiology, New York University Medical Center, New York, New York

McCune-Albright Syndrome is an uncommon chromosomal endocrine disorder characterized by polyostotic fibrous dysplasia, café au lait spots, and sexual precocity (1). Hyperthyroidism, growth hormone excess, hyperparathyroidism, hyperprolactinemia, and/or hypercortisolism may be present in any combination (1). Although the literature states that this syndrome occurs sporadically, we could not find any information about its exact incidence (2,3). Patients with this syndrome often present to the anesthesiologist for repair of bone lesion–related fractures. The scarcity of information about the anesthetic management of this disorder stimulated the preparation of this case report that describes expected and unexpected aspects of this syndrome.

Case Report

A 5-yr-old, 135-cm, 27.3-kg girl was admitted for osteotomy and intramedullary nailing of a right femur that developed a malunion after a fracture caused by polyostotic fibrous dysplasia (Fig. 1). McCune-Albright syndrome was diagnosed at 4 mo of age, when she had vaginal bleeding from onset of menses. Her pubic hair began to develop at 2 yr of age. She also exhibited the gonadotrophic changes of precocious puberty, with Tanner Stage I breast development and Tanner Stage III vaginal development (Fig. 2). Clinically she appeared to be euthyroid. She received ^{131}I therapy about 2 yr before surgery and was on a regimen of Tapazole® (Eli Lilly and Co., Indianapolis, IN), 7.5 mg three times a day; Synthroid® (Flint Laboratories, Inc., Deerfield, IL), 37.5 mg four times a day; and propranolol, 10 mg twice a day. Thyroid function studies performed at another institution 1 wk before surgery were as follows: thyroxine 6.2 μg/dL (normal range: 4.1–11 μg/dL), thyroid-stimulating hormone 3.2 mIU (normal range: 0.5–6.7 mIU), and T_3 resin uptake 30% (normal range: 20%–32%); we were not aware of these results at the time of surgery. She showed physical signs of growth hormone excess, although her growth hormone level was not measured preoperatively. She appeared to be about 8–10 yr of age and had a surprisingly deep voice. Routine airway assessment, including the extent of mouth opening, the visibility of the uvula, the hyo-mental distance, and the ability of the patient to extend her head did not suggest any difficulty with intubation. Anesthesia was induced with halothane and nitrous oxide in oxygen. The trachea was intubated with a 5.5-mm inside diameter (ID) uncuffed endotracheal tube while spontaneous ventilation was maintained. The laryngeal opening appeared to be somewhat larger than expected. Bilateral breath sounds were heard, but a large air leak was present with airway pressures less than 5 cm H_2O. The endotracheal tube was replaced under direct visualization with a 6.0-mm ID tube, but the air leak at less than 5 cm H_2O pressure remained. After several tube exchanges, a 7.0-mm ID cuffed tube finally achieved a fit that leaked at around 20 cm H_2O with the cuff deflated. The rest of the anesthetic proceeded uneventfully; no further airway evaluation was performed intra- or postoperatively. Her trachea was extubated in the operating room at the conclusion of surgery, and she was monitored closely for 24 h postoperatively. Her hospital course was uncomplicated, and her postoperative thyroid function studies remained within normal limits. She was discharged on the fifth postoperative day.

Discussion

McCune-Albright syndrome is a genetic disorder first described in 1937 (4,5). A somatic mutation during the early stages of embryogenesis leads to alteration of a gene that encodes for a protein that regulates cyclic AMP activation in affected organs (6). Somatic mutation results in a mosaicism that accounts for the heterogeneity of its manifestations. Two authors have isolated similar mutations in exons 8 and 9 of the gene encoding the alpha subunit of a regulatory G-protein (6,7). These mutations result in an amino acid substitution within the regulatory protein that in turn causes autonomous, unregulated endocrine secretion in association with suppressed levels of circulating stimulating/releasing hormones (8). The syndrome is typically not hereditary. Our patient's family tree revealed that she is the only one affected out of 18 members in three generations. Most of the reported patients have been female, although at least one male child with this syndrome has been described (9).

Precocious puberty in McCune-Albright syndrome results from autonomous ovarian steroid secretion.

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Address correspondence and reprint requests to Levon M. Capan, New York University Medical Center, 560 First Avenue, New York, NY 10016.

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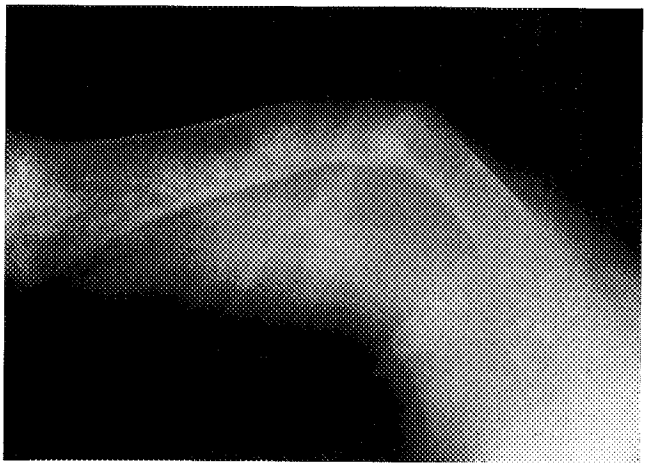

Figure 1. Left femur fracture secondary to polyostotic fibrous dysplasia.

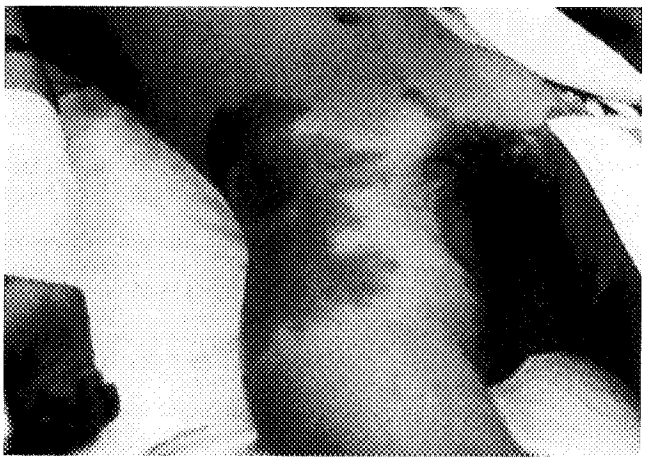

Figure 2. Photograph demonstrating the pubescent development and café au lait spots in this 5-yr-old patient.

This has been treated successfully with cyprotenone acetate (10) or medroxyprogesterone acetate (11) and does not seem to interfere with normal adult reproductive function (11–13). Hyperthyroidism is very common and can be managed medically (8,14), but it is also responsive to ^{131}I administration or thyroidectomy (14). Cushing's syndrome has been described (11) and has been treated with bilateral adrenalectomy and oral replacement therapy (14). Growth hormone excess has been successfully treated with low-dose octreotide (15) or transsphenoidal hypophysectomy (11,14).

The important anesthetic considerations are to identify the endocrine systems affected, to determine the severity of their functional derangement, and to detect any airway abnormalities that may affect management. Recognition of hyperthyroidism is of particular importance. Most patients with uncontrolled hyperthyroidism present with characteristic clinical signs and symptoms: weight loss, diarrhea, warm/moist skin, weakness of large muscle groups, nervousness, heat intolerance, tachycardia, cardiac dysrhythmias, mitral valve prolapse, and/or evidence of congestive heart failure (16–18). Thyroid function tests should be evaluated preoperatively, although the clinical status of the patient is more important than are absolute laboratory values (16). Laboratory tests may be necessary to differentiate between disorders with similar manifestations, to diagnose mild cases of hyperthyroidism with equivocal clinical presentations, and to detect possible hypothyroidism caused by antithyroid therapy (17). In the rare instances when thyroid function studies are in the upper range of normal or minimally elevated, thyroid suppression and/or thyroid releasing hormone stimulation tests may be useful in diagnosis (17). We relied on the clinically euthyroid presentation of our patient and did not insist on obtaining the results of the thyroid function tests which had been performed in another institution. However, for the reasons mentioned above, we now believe it prudent to obtain these results preoperatively. Current recommendations dictate rendering all hyperthyroid patients euthyroid with antithyroid therapy before any elective surgery (16,18). This approach decreases the likelihood of postoperative thyroid storm (16,18,19), although there are no data to support a conclusion that it is entirely eliminated. Thus, it is prudent to observe overnight those McCune-Albright patients who have previously manifested signs of hyperthyroidism, because thyroid storm typically occurs within 6–18 h after surgery (16). When the urgency of surgery does not permit preoperative optimization of thyroid function, judicious use of β-adrenergic blocking agents is necessary to blunt the hyperdynamic cardiovascular response to sympathetic stimulation (16,18,20). It is interesting to note that Bennett and Wainwright (21) successfully treated intraoperative thyroid storm, which was misdiagnosed as malignant hyperthermia (MH), with dantrolene. High levels of circulating T_4 have an effect on calcium flux across the sarcoplasmic reticulum. Thus, the dosage of dantrolene recommended for malignant hyperthermia should be effective for the hyperthermia associated with thyroid storm (21).

Although Cushing's disease was not part of our patient's syndrome, its presence may require preoperative treatment of hypertension, hyperglycemia, and/or hypokalemia (22) Chemotherapeutic agents such as metyrapone, cytoproheptadine, or bromocriptine reduce steroid secretion (23,24). Perioperative steroid administration should be considered in McCune-Albright syndrome with Cushing's disease, because these patients may have an altered cortisol response to stress (22). Vascular fragility may make venous access difficult (22). Because these patients have increased bone fragility, particular attention must be paid to

careful positioning and padding (22). Tracheal intubation may be difficult because of obesity or the development of the classic "buffalo hump." Postoperative respiratory insufficiency may result from decreased muscle mass, hypokalemia, and obesity (25).

Acromegaly may distort airway anatomy. Flexible fiberoptic laryngoscopy may be necessary for optimal management (26). One report describes a mandibular fracture from unsuccessful direct laryngoscopy in an acromegalic patient (26). The authors suggest that because patients with acromegaly commonly have decreased bone density, fracture may result from minimal stress. Conduction anesthesia may be difficult if vertebral collapse has occurred due to this abnormality.

The patient described in this report had an enlarged larynx, as demonstrated by visual inspection and a requirement for a much larger endotracheal tube than would be expected in a child of her age. The mechanism is most likely the result of growth hormone excess. Alterations in laryngeal structures reported in patients with acromegaly include accelerated laryngeal growth, laryngeal cartilage and soft tissue hypertrophy, thickening of laryngeal mucosa, and widening of the larynx (27–29). These changes decrease voice pitch, giving it a hollow quality and a coarse hoarseness (29). Hypertrophy of soft tissues in the airway may make intubation more difficult (28). Intubation of the trachea was not a problem in our patient, and thus the need to replace the endotracheal tube (ETT) several times was not associated with complications. However, in a patient who is difficult to intubate, the necessity for multiple laryngoscopies and attempts at intubation may lead to complications.

The main thrust of anesthetic management in McCune-Albright syndrome involves identification and management of associated endocrine abnormalities. Airway management may be rendered difficult by airway distortion with associated acromegaly or simply by requirement of a larger size ETT than expected. One may consider placing a cuffed ETT that can be inflated if there is a significant air leak. Age as the sole criterion for ETT size selection may not be the best approach. Luten et al. (30) suggest a method of ETT selection that uses body length, perhaps offering a more rational approach when body and laryngeal sizes exceed those predicted by age alone.

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